Title	Effect of High Tibial Osteotomy on the Distribution of Subchondral Bone Density Across the Proximal Tibial Articular Surface of the Knee With Medial Compartment Osteoarthritis
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Citation	American journal of sports medicine, 49(6), 1561-1569 https://doi.org/10.1177/03635465211002537
Issue Date	2021-05-01
Doc URL	http://hdl.handle.net/2115/82172
Rights	Koji Iwasaki, Eiji Kondo, Shinji Matsubara, Masatake Matsuoka, Kaori Endo, Isao Yokota, Tomohiro Onodera, Norimasa Iwasaki, Effect of High Tibial Osteotomy on the Distribution of Subchondral Bone Density Across the Proximal Tibial Articular Surface of the Knee With Medial Compartment Osteoarthritis, The American Journal of Sports Medicine, Vol.49(6) p. 1561-1569 Copyright © 2021 The Author(s). DOI:10.1177/03635465211002537
Type	article (author version)
File Information	AJSM HTO_Manuscripts_Final.pdf

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1 MS ID#: AMJSPORTS/2020/312314

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Effect of high tibial osteotomy on the distribution of subchondral bone density

across the proximal tibial articular surface of the knee with medial compartment

osteoarthritis

Abstract

Background: The effect of high tibial osteotomy (HTO) on the stress distribution across the knee joint is not completely understood. The subchondral bone density is considered to reflect the pattern of stress distribution across a joint surface.

Purpose: To assess the distribution of subchondral bone density across the proximal tibia in nonarthritic knees and in the knees of patients with osteoarthritis before and after HTO.

Methods: We retrospectively collected radiographic and computed tomography (CT) data from 16 nonarthritic subjects (control group) and 17 patients with OA (OA group). Data from the OA group were collected before and 1.5 year after HTO. The subchondral bone density of the proximal tibia was assessed with CT–osteodensitometry. The locations and percentages represented by high-density areas on the articular surface were quantitatively analyzed.

Results: The ratio of the high-density area of the medial compartment to the total high-density area (medial ratio) was significantly higher in preoperative OA patients (mean, 80.1%) than in control subjects (61.3%) ($p < 0.001$). After HTO, the medial ratio decreased significantly (to 75.1%, $p = 0.035$, in comparison with preoperative values) and was significantly correlated with the hip–knee–ankle angle (HKA) in both the control ($r = -0.551$, $p = 0.033$) and OA groups ($r = -0.528$, $p = 0.043$). The change in medial

ratio after HTO was significantly correlated with the change in HKA ($r = 0.587$, $p = 0.035$). In the medial compartment, the high-density area in most lateral areas of four divided subregions increased after HTO, but that of the other medial three subregions decreased.

Conclusions: In this exploratory study, HTO shifted the high-density area of the medial compartment of the proximal tibial articular surface toward the lateral compartment. In contrast, the high-density area of the most lateral region of the medial compartment decreased after HTO. This change in subchondral bone density may result from the change in stress distribution.

Clinical relevance: Assuming that the subchondral bone density is a surrogate for stress, HTO shifts the stress from the medial compartment to the lateral compartment but increases the stress on the most lateral region of the medial compartment.

Key terms: high tibial osteotomy, knee, osteoarthritis, stress distribution, CT–osteabsorptiometry, alignment

What is known about the subject: HTO has been suggested to decrease the stress on the medial compartment of the knee joint. However, the effect of HTO on the stress distribution across the knee joint is not completely understood.

What this study adds to existing knowledge: HTO decreases the stress on the medial

66 compartment of the proximal tibial articular surface and shifts the distribution of stress
67 toward the lateral compartment. Moreover, the stress on the medial compartment does not
68 decrease across the whole area after HTO and actually increases at the most lateral region.

Introduction

Biomechanical risk factors for knee osteoarthritis (OA), such as obesity, trauma, malalignment, meniscal deficiency, and muscle weakness, increase the mechanical stress across the knee joint. Some of these factors are believed to be important and potentially modifiable factors that determine the site⁴⁵ and severity⁴⁵ of knee OA. Identifying the distribution of mechanical stress across the knee joint would thus contribute to the prediction and management of OA progression.

Malalignment of the lower limbs is a strong risk factor for progression of knee OA, and one of the few risk factors that can be modified *a posteriori*. Valgus high tibial osteotomy (HTO) is an established surgical procedure that can be used to treat medial knee OA. HTO reduces loading of the medial compartment and, thereby, slows disease progression. Because it extends the healthy life expectancy of the knee, HTO is widely used as a treatment option for medial OA with varus alignment.^{3, 10, 16} The relationships among leg alignment, medial compartment loading, and change in medial compartment loading after HTO have been examined in a cadaveric study,¹ finite element analyses,^{36, 52} and three-dimensional (3-D) gait analyses by assessing the knee adduction moment (KAM)^{7, 15, 29}; however, how the distribution of the actual stress within each compartment changes after HTO remains unclear.

The distribution of the subchondral bone mineral density is thought to be correlated with the distribution of stress over the joint surface; because of the varying degrees of mineralization over the surface of a joint, a materialized field of stress is observed.⁴² Computed tomography (CT)–osteabsorptiometry was developed by Müller-Gerbl et al. as an analytical method to assess the long-term stress distribution over individual joints in living participants by measuring the subchondral bone mineral density.^{31, 32} This method generates a precise map of the distribution pattern of subchondral bone density over various articular surfaces. Our previous studies involving this method have evaluated the distribution of subchondral bone density to assess the pattern of stress distribution at the wrist, elbow,³⁴ and the glenohumeral,^{12, 46} patellofemoral,³⁷ and ankle joints⁴¹ in normal people, those with pathological conditions, and athletes. The distribution pattern of subchondral bone density over the knee joint has been suggested to be related to the presence of knee OA^{19, 39}; however, it is unclear whether leg alignment affects the distribution of bone density. Furthermore, whether or how the distribution pattern of subchondral bone density changes on the articular surface across the knee joint after HTO is yet to be elucidated.

Using CT–osteabsorptiometry, a precise map of the subchondral bone density distribution across the knee joint could provide insight into the stress distribution across

the articular surface of the knee joint with and without OA and the change in the stress distribution after HTO. Thus, we hypothesize that valgus HTO leads to a reduction in the *in vivo* subchondral bone density on the medial compartment of the femorotibial joint in the case of varus OA of the knee. The aims of this exploratory study were: (1) to evaluate the distribution pattern of subchondral bone density across the proximal tibia in patients with and without OA, (2) to assess changes in the pattern of bone density distribution in patients with OA before and after HTO, and (3) to clarify the correlation of leg alignment with changes in bone density distribution.

Methods

Study design

This study was approved by the institutional review board of Hokkaido university hospital (017-0163). We retrospectively recruited all patients who underwent HTO for medial compartment OA between April 2013 and March 2017 at our institution. All operations were performed by a senior orthopedic surgeon (EK) who had over 20 years of experience in performing knee surgery. The OA group included patients who underwent medial open wedge HTO (OWHTO) for medial compartment OA. Indications for OWHTO in our hospital were: (1) moderate varus leg alignment (HKA of $>-10^\circ$) and (2) absence of OA in the patellofemoral joint (Kellgren–Lawrence [KL] grade²¹ $\geq$ II) or

123 anterior knee pain. Exclusion criteria were: (1) lateral knee OA (KL grade $\geq$ II) or lateral
124 knee pain, (2) not completing a follow-up period of at least 1 year, (3) having no metal
125 removal after HTO, (4) loss of $>15^\circ$ of knee extension before and after HTO, (5) knee
126 range of motion of $<130^\circ$ before and after HTO, (6) anterior cruciate ligament
127 insufficiency or varus/valgus instability of $>10^\circ$, (7) medial meniscal injury $\geq$ grade 3
128 (Lotysch and Mink's magnetic resonance imaging [MRI] grading system^{5, 30}) or any tear
129 of the medial meniscus for which partial meniscectomy or other repair was performed,
130 and (8) any lateral meniscal injury. Finally, we evaluated 17 knees in 16 patients in the
131 OA group (Figure 1).

Figure 1. Flowchart of study enrollment

Abbreviations: HTO, high tibial osteotomy; OA, osteoarthritis; OWHTO, open wedge HTO.

We also collected the data of 16 patients who underwent simultaneous radiographical and CT examinations of bilateral knees for comparison of ipsilateral knee trauma between April 2013 and March 2017 as control subjects. The uninjured contralateral knee was used as control. Inclusion criteria for the control group were (1)

knee OA (KL grade ≤ 1) in the contralateral knee and (2) patients aged 15–30 years at the time of CT scanning. Exclusion criteria for the control group were (1) current pain in the contralateral knee and (2) previous surgery in the contralateral knee.

Postoperative clinical and radiological evaluations were performed around 1.5 years (mean: 17.4 months, range: 14–25 months) after OWHTO and immediately after removal of the locking plate.

Preoperative planning

Miniaci's method was used for preoperative planning as previously reported.^{33, 43, 49} To calculate an appropriate angle of the medial opening wedge, a long line, [A], was drawn from the center of the femoral head through the 65% lateral from the medial edge of the tibial plateau on the lateral tibial plateau. Another line, [B], was then drawn from the hinge point [P] to the center of the talar dome, and its length was measured. An arc, [C], the center and the radius of which are the hinge point P and line B, respectively, was then drawn so that the arc crossed line A. A line, [D], was then drawn from the hinge point to the crossing point between line A and the arc C. The angle formed between lines B and D provides the medial opening angle, which is identical to the correction angle of the lower limb alignment.

Surgical technique

Surgery was performed as previously described.^{40, 43, 49} The proximal tibia was

exposed through a 7-cm medial longitudinal incision. Further, after the complete release of the distal attachment of the superficial medial collateral ligament, three pairs of Kirshner wires (K-wires) were inserted into the tibia so that each inserted K-wire precisely reached the proximal tibiofibular joint using the parallel guide. We then performed a biplanar osteotomy of the tibia, after which the oblique osteotomy site was gradually opened—according to the preoperative planning angle—using a specially-designed spreader (Olympus Terumo Biomaterials, Tokyo, Japan). Under fluoroscopic control, we set a long straight metal rod to connect the center of femoral head and ankle, then measured the transection point of the rod through the tibial plateau. This was expressed as a percentage of the tibial width from medial-to-lateral. We confirmed the transection point of 65%.¹¹ Two wedged beta-tricalcium phosphate spacers (Osferion 60; Olympus Terumo Biomaterials) were implanted into the anterior part and posterior part of the opening space in a parallel fashion. We fixed the tibia with a locking plate (Tomofix; DePuy Synthes, Raynham, MA, USA, or TriS Medial HTO plate system; Olympus Terumo Biomaterials) by inserting eight locking screws.

Each patient underwent an additional procedure approximately 1 year (mean: 13.4 months, range: 12–15 months) after the initial surgery to remove the locking plate. Arthroscopic evaluation was performed simultaneously to evaluate the status of the

meniscus after HTO.

Evaluation criteria

Clinical evaluation

Patients were evaluated according to the Japanese Orthopaedic Association (JOA) knee scoring system (total, 100 points),^{4, 50} which is the standard knee subjective score used in clinics in Japan. The JOA knee score consists of four categories: “pain on walking” (0–30 points), “pain on ascending and descending stairs” (0–25 points), “range of motion” (0–35 points), and “joint effusion” (0–10 points).

Meniscus status evaluation

To compare meniscus status before and after HTO, an examiner (KI) evaluated the arthroscopic images at HTO as well as at plate removal and MRI images before HTO as well as after plate removal according to the Lotysch and Mink’s MRI grading system.³⁰ The change in meniscal status after HTO was graded according to three categories: deterioration, no change, and improvement.

Radiological evaluations

Standing anteroposterior and lateral radiographs of the knee and full-length anteroposterior radiographs of the whole lower limb with the knee in full extension were

acquired. The radiological stage of OA was assessed according to the KL grading system.²¹ We measured HKA on anteroposterior radiographs of the whole lower limb taken with a long cassette in the one-leg standing position. We also calculated the percentage of mechanical axis (%MA) as follows: A line was drawn between the center of the femoral head and the center of the tibial plafond; the medial edge of the tibia plateau was defined as 0% and the lateral edge as 100%, and the %MA was the point at which the line passed across the tibial plateau.^{8, 20, 35, 38, 51} The posterior tibial slope (PTS) was measured as the angle between a line perpendicular to the mid-diaphysis of the tibia and the posterior inclination of the medial tibial plateau on the lateral view.

Computed tomography–osteabsorptiometry

A high-resolution helical CT scanner (Aquilion One/ViSION Edition; Toshiba Medical Systems, Japan) was used to acquire axial images of the knee. Patients rested in a supine position with their knees extended during imaging. Slice thickness and interval were set at 0.5 mm. Acquired CT data were transferred to a personal computer. Sagittal and coronal slices at 1.0-mm intervals and 3-D bone models were generated from axial CT data with the use of commercial software (Ziocube®; Ziosoft, Inc., Tokyo, Japan). We determined the sagittal and coronal axes by reference to the epicondylar axis of the

214 distal femoral condyle at the axial slice. By reference to sagittal and coronal CT images
215 and a 3-D CT image of the articular surface of the proximal tibia, an outline of the medial
216 and lateral compartment of proximal tibial articular surface was manually selected to
217 include the entire subchondral bone layer of the articular surface in all slices.¹² Then the
218 subchondral bone density of each generated sagittal slice was analyzed with our
219 noncommercial software (OsteoDens 4.0) developed at our institution.^{12, 17, 37, 41, 46} The
220 maximum increment point in Hounsfield units from the joint surface as the starting point
221 of the region of interest, and the maximum point in Hounsfield units was selected
222 automatically in the 2.5-mm region of interest from the starting point (Supplementary
223 file). We determined the radiodensity of the identified subchondral bone region at each
224 coordinate point at 1-mm intervals. Then, a two-dimensional image that mapped the
225 distribution of subchondral bone density was obtained by stacking sagittal slices (Figure
226 2A, 2B). The differences between the maximum and minimum values in Hounsfield units
227 on the mapping images were divided into nine grades, and a surface mapping image was
228 generated through the use of these grades to produce a color scale, in which red and violet
229 indicated the greatest and lowest bone densities, respectively. Selected areas of the medial
230 and lateral plateaus included the cortical bone or bony spur at the periphery of the articular
231 surface because it was impossible to exclude the cortical bone or bony spur using the

software. However, these features were carefully removed manually from the target area of analysis in subsequent quantitative analysis.¹²

Quantitative analysis of the obtained mapping data focused on the location of the high-density area (HDA) of the articular surface. The HDA was defined as the region containing the coordinate points representing the top 20% of Hounsfield unit values out of the total area of the medial and lateral compartments. The medial ratio was calculated as the ratio of the HDA of the medial compartment to the total HDA of both compartments. The medial compartment of the proximal tibia was divided into four subregions of equal width in the coronal direction, denoted M1 to M4 from the medial-to-lateral sides. The lateral compartment was divided equivalently, denoted L1 to L4 from the medial-to-lateral sides (Figure 2C). The percentage of each subregion represented by the HDA was calculated (%HDA).

Figure 2. Identification of the subchondral bone regions of the proximal tibia using a customized software. (A, B) The subchondral bone density of the selected region was automatically measured at each coordinate point in each 1.0-mm sagittal slice. (C) Images of the areas used for quantitative analysis of the bone density mapping data for the medial and lateral compartments of the proximal tibia.

Definitions: M1–M4, subregions of the medial compartment of the proximal tibia, divided equally from the medial side to the lateral side; L1–L4, subregions of the lateral compartment, divided equally from the medial side to the lateral side.

Statistical analysis

Statistical analyses were performed using JMP Pro 14.0 (SAS Institute Inc., Cary, NC, USA). The significance level was set at $p = 0.05$. Means and 95% confidence intervals (CIs) for the changes after surgery in patients with OA were calculated. We compared controls and patients with OA before and after surgery by using Student's t test, and we compared the patients with OA before and after surgery by using a paired t test. Pearson's correlation was used to evaluate the relationship between medial ratio and other factors (age, body mass index [BMI], HKA, %MA, and PTS) to compare controls with preoperative patients. In addition, we compared changes from preoperative to postoperative values (denoted by " Δ ") of the medial ratio and other variables using Pearson's correlation. These factors were selected because they are believed to influence the distribution of subchondral bone density^{19, 45, 47} or the biomechanics of the knee joint.⁴⁴

The reproducibility of data was evaluated using our noncommercial software (OsteoDens 4.0). Intra- and interobserver reliability were assessed on three randomly selected knees from the control group and each OA group. Two observers (KI and SM)

independently measured %HDA in these six knees; a total of 48 subregions were measured twice in a blinded manner at 1 month intervals. The intraclass correlation coefficients for intraobserver reliability were 0.922 (KI) and 0.913 (SM), respectively, and the intraclass correlation coefficient for interobserver reproducibility was 0.917.

Results

Age, BMI, HKA, and %MA were significantly different between the control and preoperative OA groups ($P < .001$, $P = .026$, $P < .001$, and $P < .001$, respectively; Table 1). The medial ratio was 31% higher in the preoperative OA group than in the control group ($P < .001$).

After HTO, JOA score improved by 33% ($P < .001$). The sum of “pain on walking” and “pain on ascending and descending stairs” subcategory scores improved by 56% ($P < .001$). Significant differences in HKA, %MA, and PTS between the preoperative and postoperative OA groups ($P < .001$, $P < .001$, and $P = .019$, respectively). The medial ratio decreased by 6% after HTO, respectively ($P = .035$; Table 1).

In the comparison between the patients with OA after surgery and the controls, leg alignment was significantly more valgus in the patients (5.0 degrees valgus in HKA) compared with the controls (1.5 degrees varus; $P < .001$). The medial ratio was 21%

288 higher in the patients than that in the controls ($P = .008$).

289 Table 1. Patient characteristics, OA grade, leg alignment, clinical outcomes, and medial

290 ratio^a

Characteristic	Controls (n = 16)	Patients with OA (n = 17)		Comparison: on: preop with control	Comparison: preop with postop		Comparison : postop with control
		Preoperative	Postoperative	<i>P</i> value	Mean change	<i>P</i> value	<i>P</i> value
Age, years	20.8 (18.1– 23.4)	58.9 (54.8– 63.0)	n/a	<.001	n/a	n/a	n/a
Male:female ratio	8:8	6:11	n/a	.393	n/a	n/a	n/a
BMI, kg/m ²	24.0 (21.8– 26.2)	27.0 (25.1– 28.9)	n/a	.026	n/a	n/a	n/a
KL grades (III and IV)	n/a	16:1	16:1	n/a	n/a	.99	n/a
HKA, degrees	−1.5 (−3.4– 0.4)	−6.1 (−8.0– −4.2)	5.0 (4.1– 5.8)	<.001	9.9 (7.6– 12.2)	<.00 1	<.001
%MA, %	43.8 (37.3– 50.3)	22.8 (14.9– 30.7)	68.8 (65.3– 72.3)	<.001	45.4 (36.7– 54.0)	<.00 1	<.001
PTS, degrees	9.9 (8.2– 11.6)	11.5 (9.7– 13.7)	13.1 (10.8– 15.4)	.191	1.6 (0.3– 2.8)	.019	.025
JOA knee score, points							
Total	n/a	68.8 (61.3– 76.2)	91.6 (86.6– 96.5)	n/a	22.7 (17.3– 28.3)	<.00 1	n/a

Pain on walking	n/a	19.6 (17.2–21.9)	29.1 (27.7–30.5)	n/a	9.6 (6.8–12.3)	<.001	n/a
Pain on ascending and descending stairs	n/a	13.6 (11.0–16.3)	22.7 (21.0–24.5)	n/a	9.1 (6.5–11.6)	<.001	n/a
Range of motion	n/a	28.6 (26.5–30.8)	30.9 (28.4–33.4)	n/a	2.3 (0.5–4.0)	.02	n/a
Joint effusion	n/a	6.8 (4.6–9.1)	8.3 (7.1–10.2)	n/a	1.8 (0.1–3.5)	.04	n/a
Medial ratio, ^b %	61.3 (55.7–66.9)	80.1 (72.3–85.6)	75.1 (67.8–83.5)	<.001	4.4 (0.6–8.1)	.035	.008

291 ^aData are reported as means (95% confidence intervals) or ratios.

292 ^bMedial ratio: The ratio of high-density area (HDA) of the medial compartment in relation
293 to the total HDA of both compartments. HDA: 20% highest area in Hounsfield unit values
294 out of the sum of the medial and lateral compartments. Varus alignment was a negative
295 value of HKA, and valgus alignment was a positive value.
296 n/a, not applicable. OA, osteoarthritis. BMI, Body mass index. KL, Kellgren–Lawrence.
297 HKA, Hip–knee–ankle angle. %MA, Percentage of mechanical axis. PTS, Posterior tibial
298 slope. JOA, Japanese Orthopedic Association (knee score: total, 100 points). Preop:
299 before HTO. Postop: 1 year after HTO.

300 In arthroscopic evaluation after HTO, meniscal status was graded “no change”
301 in both medial and lateral compartments in all cases. However, Lotysch and Mink’s MRI
302 grading of meniscal status was unchanged in both medial and lateral compartments after
303 HTO.

304 Of the parameters that differed significantly between the control and
305 preoperative OA groups, age, HKA. and %MA were found to be significantly correlated
306 with the medial ratio (Table 2). Only HKA was found to be significantly correlated with

the medial ratio in both the control and OA groups (Figure 3).

Table 2. Statistical analysis: Pearson correlation (r) between medial ratio and demographic data in controls and patients with osteoarthritis^a

Characteristic	Controls		Patients	
	r	P value	r	P value
Age	0.122	.670	0.671	.009
BMI	−0.144	.609	−0.077	.785
HKA	−0.551	.033	−0.528	.043
%MA	−0.558	.031	−0.432	.108
PTS	−0.126	.654	−0.217	.438

^aMedial ratio: The ratio of high-density area (HDA) of the medial compartment relative to the total HDA of both compartments. HDA: 20% highest area in Hounsfield unit values out of the sum of the medial and lateral compartments.

BMI, Body mass index. HKA, Hip–knee–ankle angle. %MA, Percentage of mechanical axis. PTS, Posterior tibial slope.

Figure 3. Relationship between hip–knee–ankle angle (HKA) and medial ratio. (A) Control group: Pearson correlation analysis showing a significant negative correlation between HKA and medial ratio (Pearson $r = -0.551$; $P < 0.033$). (B) OA group: Pearson correlation analysis showing a significant negative correlation between HKA and medial ratio (Pearson $r = -0.528$; $P < 0.043$). Medial ratio: The ratio of high-density area (HDA) of the medial compartment in relation to the total HDA of both compartments. HDA: 20% highest area in Hounsfield units values out of the sum of the medial and lateral compartments.

Of the patients' characteristics, including age, BMI, sex, and JOA knee score, none showed a significant correlation with Δ medial ratio. In contrast, of the parameters that were changed after HTO, only Δ HKA was significantly correlated with the Δ medial ratio ($P = .035$; Table 3). In addition, there was no significant correlation between Δ HKA and functional knee score.

Table 3. Statistical analysis: Pearson correlation coefficients and partial correlation coefficients between Δ medial ratio and demographic data in patients with osteoarthritis before and after HTO^a

Characteristic	Correlation coefficient	<i>P</i> value	Partial correlation coefficient
Pre-HTO HKA	-0.338	.259	-0.431
Pre-HTO PTS	0.0002	.999	0.151
Post-HTO HKA	0.432	.140	0.415
Post-HTO PTS	0.009	.999	0.031
Δ HKA	0.587	.035	0.539
Δ PTS	0.018	.930	0.151

^a Medial ratio: The ratio of high-density area (HDA) of the medial compartment in relation to the total HDA of both compartments.

HDA: 20% highest area in Hounsfield unit values out of the sum of the medial and lateral compartments. HTO, High tibial osteotomy. HKA, Hip-knee-ankle angle. PTS, Posterior

337 tibial slope. Post-HTO refers to 1 year after HTO. Δ : the value of the change before and
 338 after HTO.

339 Subregional %HDA analysis revealed %HDA of the M2 and M3 regions to be
 340 significantly higher among patients with OA than controls ($P = .011$ and $P < .001$,
 341 respectively). The %HDA of all four subregions of the lateral compartment was
 342 significantly lower in patients with OA than controls (for M1, $P < .001$; for M2, $P = .013$;
 343 for M3, $P = .005$; and for M4, $P = .005$; Table 4). After HTO, the %HDA of M2 and M3
 344 decreased by 23% ($P = .009$) and 20% ($P = .017$), respectively. whereas that of M4
 345 increased by 19% ($P = .014$). In the lateral compartment, the %HDA of L2 and L3
 346 increased by 52% ($P = .026$) and 74% ($P = .006$).

347 Table 4. Subregional analysis of %HDA^a

Subregion	Controls	Patients with OA		<i>P</i> value	
		Preoperative values	Postoperative values	Comparison: Preop with control	Preop–postop change
M1	6.2 (4.6–7.9)	9.5 (6.5–12.6)	7.0 (3.9–10.2)	.051	.112
M2	18.9 (16.4–21.3)	23.4 (20.8–26.0)	18.1 (13.8–22.5)	.011	.009
M3	21.6 (19.8–23.3)	29.0 (26.5–31.6)	23.2 (18.5–28.0)	<.001	.017
M4	16.1 (13.0–19.1)	18.1 (15.1–21.0)	21.6 (18.3–24.9)	.323	.014
L1	12.1 (9.9–14.3)	5.4 (3.5–7.3)	8.1 (4.0–12.1)	<.001	.132
L2	13.5 (11.4–15.6)	9.1 (6.3–12.0)	13.8 (9.4–18.3)	.013	.026
L3	9.0 (6.6–11.4)	4.2 (1.8–6.6)	7.3 (3.7–10.9)	.005	.006
L4	2.7 (1.2–4.2)	0.5 (0.1–0.8)	1.6 (0.2–3.0)	.005	.095

348 ^aData are reported as means (95% confidence intervals).

HDA: 20% Highest area in Hounsfield unit values out of the sum of the medial and lateral compartments. %HDA: The percentage of the HDA in each subregion. OA, osteoarthritis. HTO, High tibial osteotomy. Preop: before HTO. Postop: 1 year after HTO. M1–M4: Subregions of the medial compartment of the proximal tibia, divided equally from the medial side to the lateral side. L1–L4: Subregions of the lateral compartment, divided equally from the medial side to the lateral side.

Discussion

In this study, we demonstrated that the medial ratio, defined as the ratio of the medial HDA to the total HDA of the proximal tibia, was increased among patients with OA and varus deformity but decreased significantly after valgus HTO. Furthermore, we discovered that leg alignment was significantly correlated to medial ratio in healthy individuals as well as patients with OA and that the degree of correction of alignment after HTO was correlated to the change in medial ratio.

According to the results of previous studies involving dual-energy X-ray absorptiometry (DEXA), leg alignment was correlated with bone mineral density (BMD) of the proximal tibia^{2, 25, 47} as well as with the decrease in BMD of the medial compartment after HTO.^{2, 25} These findings are similar to the results of our study. However, DEXA is used to evaluate BMD of the periarticular bone but does not distinguish the subchondral bone plate from trabecular bone of the articular surface or from bone spurs or cortical bone. In addition, according to the results of one experimental

study, BMD of subchondral bone and trabecular bone changed differently over time,⁶ which suggests the difficulty of evaluating the change in the BMD of subchondral bone precisely with DEXA. In contrast, in CT–oste absorptiometry, bone spurs can be hidden in the region of interest so that the focus is on the subchondral bone plate of the articular surface. This was believed to be an advantage in our study.

Previous studies involving CT–oste absorptiometry have indicated that the distribution pattern of subchondral bone density reflects the distribution of the resultant stresses acting on a joint surface under actual loading conditions.^{12, 17, 18, 31, 32, 34, 37, 41, 46} We found the medial ratio to be higher in OA patients than healthy individuals, decreasing after HTO in the former. Moreover, the JOA knee scores improved, particularly in the pain subcategories, after HTO. These results indicated that HTO reduces the stress distribution pattern across the medial compartment of the proximal tibial articular surface.

The correlation between Δ HKA and Δ medial ratio was weak ($r = 0.587$), which indicates that the change in leg alignment explained the small variance ($\sim 35\%$) in the Δ medial ratio. Other factors not evaluated in this study, including physical characteristics (e.g., muscle strength, pelvic width), kinetics (i.e., dynamic alignment), and postoperative activity, might explain the rest of the variance in the Δ medial ratio. Our results demonstrated that HKA, but not age and BMI, was significantly correlated with the

medial ratio in both healthy individuals and patients with OA, and that only Δ HKA was significantly correlated with the Δ medial ratio among variances (age, sex, BMI, JOA knee score, and pre-, postoperative and Δ values of HKA and PTS). In addition, a 3-D motion analysis study demonstrated that among the changes in the mechanical axis angle, PTS, gait speed, and lateral trunk lean, only the change in the mechanical axis angle was significantly correlated with the change in KAM during level walking before and after HTO.²⁸ Thus we can conclude that leg alignment is an important factor influencing the stress distribution pattern across the proximal tibial articular surface.

The comparison between the patients postoperatively and the controls revealed that although the patients had valgus alignment more than did controls, the medial ratio was still higher in the patients postoperatively. A possible explanation for this dissociation between the alignment and the medial ratio is the influence of OA itself on the subchondral bone density.^{19, 39} Another possible explanation is that the distribution of bone density 1.5 years after HTO was not the final distribution of bone density after HTO, inasmuch as the DEXA study mentioned earlier demonstrated that a medial-to-lateral ratio of femoral and tibial condyle BMD was still changing 1 year after HTO.²⁵ Further study is needed to clarify when the final distribution of subchondral bone density is established.

The results of our subregional analysis of HDA distribution pattern before and after HTO demonstrated that, of the four subregions in the medial compartment, %HDA of M2 and M3 decreased after HTO, whereas M4 was the only region of the medial compartment to exhibit increased %HDA. These results suggested that stress on the most lateral region of the medial compartment increases after HTO. A finite element study has reported that shear stress on the lateral region in the medial compartment increases as lateral joint line obliquity increasing.³⁶ This might be a reason for the paradoxical observation that the stress increases on the most lateral region only but decreases for all other regions. Further study is required to clarify whether this effect influences long-term clinical outcomes; however, surgeons should consider the risk of progression of OA at the most lateral region of the medial compartment after HTO due to increased mechanical stress, especially in cases where changes in OA have occurred in this region. In this study, the mean medial ratio was higher in the OA (80.1%) than control group (61.3%), which is consistent with a previous biomechanical study in which the percentage of total loading attributable to medial compartment loading was 66% in the control group (with normal alignment) compared with 74.5% in patients with OA at the first peak of the KAM.²⁶ The similarity between the medial ratio of this study and the medial compartment loading ratio in the previous study²⁶ provides some support and verification of the reliability of CT–

osteoaabsorptiometry as a method for evaluating stress distribution.^{12, 17, 18, 31, 32, 34, 37, 41, 46}

There are different opinions about the leg alignment after HTO. Some authors recommend HKA of 3°–5° valgus,^{13, 14} others suggest 8°–10° valgus.^{9, 24} Fujisawa et al. suggests %MA of 65%–70%.¹¹ However, the medial compartment loading correlated with the tibiofemoral alignment in the dynamic single-limb loading ($R^2 = 0.59$) with varus malalignment,²⁷ indicating that same leg alignment does not indicate the same distribution pattern of the joint loading. Therefore, it is thought to be desirable that the postoperative leg alignment of each patient is decided considering the distribution of the joint loading. Further investigation including of the distribution pattern of subchondral bone density and kinematic analysis including KAM can be useful for elucidating the optimal leg alignment of each patient who underwent HTO.

This study has several limitations that should be acknowledged. First, we did not directly measure the stresses and the overall bone density in the knee. Instead, the distribution of subchondral bone density in the knee joint was assessed according to the CT–osteoaabsorptiometry method.^{31, 32} Furthermore, the absolute value of stress at each analysis point was not elucidated. Therefore, it should be kept in mind that the stress distribution evaluated by the CT–osteoaabsorptiometry method does not reflect actual stress at the analysis points. Second, there was a significant difference in age between the

442 OA and control groups (mean difference 38.1 years). This study reveals that age is
443 correlated with the medial ratio in patients with OA but not in healthy individuals.
444 However, leg alignment was found to be correlated with medial ratio in both groups. This
445 indicates that age might influence the distribution of subchondral bone density as strongly
446 as varus alignment. Third, we evaluated patients with OA after the removal of metal
447 component. Finite element analysis has been used to demonstrate the stress shielding
448 effect of the HTO plate on the bone around the plate²²; however, the mechanisms
449 underlying this effect on the articular surface are unclear. Moreover, regardless of the
450 stress shielding effect of the HTO plate, this study reveals that the distribution of
451 subchondral bone density differs significantly before and 1.5 years after HTO. A fourth
452 limitation was the small sample size. We included the patients who underwent OWHTO
453 and excluded those with meniscus injury, joint instability, patellofemoral OA, and lateral
454 OA. Our results may have consequently been affected by the inclusion of patients only
455 with good outcomes, especially in view of the small sample size. At our institution,
456 however, we perform closed HTO²³ for patients with severe varus OA ($\text{HKA} \leq -10^\circ$) or
457 patellofemoral OA (KL grade $\geq$ II). In general, closed HTO necessitates fibular osteotomy,
458 which itself might affect stress distribution across the knee joint.⁴⁸ Each exclusion
459 criterion was believed to be a contraindication to HTO or a factor other than HTO that

affects the stress distribution. We thus believed that the inclusion and exclusion criteria were necessary for this study to evaluate the influence of HTO alone on the distribution of subchondral bone density as accurately as possible. Despite these limitations, the results presented here provide fundamental clarification of the stress distribution over the knee joint.

In conclusion, we demonstrated that the distribution pattern of the HDA shifted from the medial-to-lateral compartment after HTO. We discovered that leg alignment was correlated with the distribution of subchondral bone density among nonarthritic individuals and patients with OA, and that the degree of alignment correction after HTO was correlated with the change in the distribution of the HDA. Moreover, we found that the HDA of the most lateral region in the medial compartment decreased after HTO.

These findings suggest that HTO reduces the stress on the medial compartment of the proximal tibial articular surface in knees with varus OA by shifting the stress toward the lateral compartment, and that the stress on the most lateral region of the medial compartment increases after HTO, inasmuch as the change in subchondral bone density results from the change in stress distribution.

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